IN THE CLAIMS:

1-13. (Cancelled).

14. (Currently Amended) A method to analyze differential gene expression in human tissue samples derived from different biological conditions comprised of the steps of:

containing ~~providing~~ at least two samples from a human, wherein the at least two samples are comprised of proteins expressed as gene products in distinct biological conditions,

containing the proteins in discrete areas of an array that physically separate the at least two samples,

providing a plurality of antibodies wherein each member of the plurality of antibodies is identified as having specific binding affinity to an expression product of a gene sequence,

contacting each of the at least two samples with the member of the plurality of antibodies at the discrete areas of the array,

detecting an antibody-binding reaction between the member of the plurality of antibodies and the proteins contained at the discrete areas of the array, and

identifying differential gene expression between the at least two distinct biological conditions by correlating differences in the antibody binding reaction in the at least two samples with expression of the gene sequence identified with the member of the plurality of antibodies.

15. (Currently Amended) The method of claim 14 wherein the step of providing a plurality of antibodies is comprised of obtaining *in vivo* expression of the gene sequence to yield murine polyclonal antibodies having specific binding affinity to the expression product of the gene sequence.

16. (Currently Amended) The method of claim 14 wherein the step of contacting the at least two samples with the member of the plurality of antibodies is ~~comprised~~ performed on at least 100 samples.

17. (Previously Presented) The method of claim 14 wherein the step of providing at least two samples that exhibit differential gene expression is comprised of providing a first sample comprised of protein extract from normal human tissue and a second sample comprised of protein extract from a diseased sample of the same tissue.

18. (Previously Presented) The method of claim 17 wherein the second sample is protein extract from cancer cells or tissue.

19. (Previously Presented) The method of claim 17 wherein the diseased sample results from exposure to a chemical agent.

20. (Previously Presented) The method of claim 18 wherein the identifying step is comprised of identifying genes that are differentially expressed in cancerous tissue.

21. (Previously Presented) The method of claim 14 further comprising the step of identifying the expression product of the gene sequence.

22. (Cancelled)

23. (Cancelled)

Resolution of Issues Under 35 USC § 112

Claims 22 and 23 are cancelled without prejudice. Although Applicant does not acquiesce in the rejection, Applicant is canceling the claims to expedite prosecution of the application. Referring to paragraph 11 of the Action, the term "a gene sequence" in claim 14 is not vague or indefinite. The claim specifically contains the phrase "an expression product of a gene sequence." Thus, the meaning is clear that terms "gene sequence" does not refer to any specific sequence, but merely to define the source sequence that is fundamental nature of differential gene expression.

Claims 21 and 23 are not vague and indefinite or in conflict with claim 14. In the method of claim 14, differential gene expression is identified by correlating the differences between the antibody binding and the two distinct biological conditions. The advantage of this embodiment of the invention is that the expression products need not be identified prior to practicing the claimed method. The method, in fact, measures differential gene expression without the need to ever sequence an expression product because the antibodies are directly derived from expression of a large number of gene sequences. Thus, claim 14 does not conflict with claim 21, but complements it with the added limitation of actually identifying the expression product.

Regarding claims 15 and 16, two corrections are made of typographical errors: the reference to claim 1 in claim 15 is corrected and the term "comprised" is removed from claim 16..

Iris et al. Does Not Identify Differential Gene Expression by the Binding Reaction Between an Antibody and a Human Protein.

As Applicant noted in the previous response, the main focus of Iris et al. is detection of single nucleotide polymorphisms (SNPs). In order to anticipate the present claims, Iris et al would have to disclose each individual element of the presently claimed method in the same configuration and sequence of steps as in the present claims. Accordingly, the disclosure of the Iris et al reference must be carefully reviewed for each element of the pending claims. Upon a detailed review, Iris et al. do not disclose each individual element of the claimed methods. Specifically, Iris et al. does not disclose a binding reaction between an antibody that is specific for the expression product of a gene sequence and a protein present in a human patient sample that is contained in an array such that differentially expressed genes are identified. This element of the claimed method is simply not disclosed by Iris et al. who use antibody arrays having individual antibodies with distinct affinities at defined locations of the array. The expression analysis provided by Iris et al. is derived from the detection of polypeptide linked probes at the sites. Applicants obtain differential expression analysis by the difference between binding reactions in the two sample populations recited in the claims. This approach is different than Iris et al. and this element of the claim is not disclosed by the Iris et al reference.

As the Examiner notes in reference to the portions of Iris et al. cited in the action, detect a signal indicating the presence of an antibody bound to a peptide linked oligonucleotide probe. Iris et al. do not disclose a binding reaction to identify differential gene expression between two human samples. As indicated in claim 1, the present invention is different because it detects differential gene expression based on the presence of differentially expressed proteins present in tissues from different biological conditions.

Furthermore, in Iris et al., the solid phase comprises a plurality of loci, wherein each locus comprises an antibody specific to one or more of the peptide labels of oligonucleotide probes. In

contrast, the method claimed in the present invention isolates and physically separates different samples to be contacted with one given antibody, i.e., the member of the plurality of antibodies as claimed, which is an antibody against a known or unknown polypeptide expressed by an identified gene sequence. In the claimed invention, the antibody-protein binding reaction identifies the gene sequence because each antibody identifies a gene sequence. Not so with Iris et al., where the method requires nucleic acid hybridization to distinguish the SNP.

In Iris et al., the binding reaction only fixes a labeled probe, no information is conveyed by the reaction. In the present invention, the antibody-protein reaction actually identifies the differential gene sequences expressed. This element is explicitly recited in the new claims and is nowhere found in Iris et al.

Bandaru Does Not Disclose Each Element of the Pending Claims

Bandaru does not disclose the step of containing human protein samples in an array. At the cited section of Bandaru (column 4, lines 35-48), Bandaru bind capture probes to the addresses of an array, but state that "each address of the plurality having a unique capture probe... ." The reference to column 32 of Bandaru is to binding assays for the 22109 protein and does not refer to the analysis of gene expression. The only reference to gene expression analysis of proteins in tissue samples is at column 49 (bottom) to column 50 (top) where the analysis appears to be exclusively performed on a nucleic acid. Gene expression information in a tissue sample is derived from the differential binding reactions at two discrete sites of the array.

Wagner et al Does Not Anticipate the Presently Claimed Method

Referring to column 37 of Wagner et al., Wagner et al do not perform the method step of containing two tissue samples onto an array to obtain gene expression analysis. Wagner et al. distinguish their two samples using two identical arrays. Applicants specifically claim the contrary approach using two samples contained in discrete areas of the array.

None of the above references meet the limitations of dependent claim 15 wherein antibodies are raised by in vivo immunization of a gene sequence.

In light of the above, applicant requests favorable consideration and allowance of all of the newly presented claims. If the Examiner has any questions regarding the foregoing, or if the Examiner believes that an interview would facilitate the examination of this application, or if any additional information is required, the Examiner is invited to contact the undersigned at 949/567-6700, X 7740.

The Commissioner is authorized to charge **$210.00** for the two month extension fee to ORRICK, HERRINGTON & SUTCLIFFE LLP's Deposit Account No. 150665 and to credit any overpayments to said Deposit Account No. **150665**.

Respectfully submitted,

ORRICK, HERRINGTON & SUTCLIFFE LLP

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By: _____

Kurt T. Mulville
Reg. No. 37,194

4 Park Plaza, Suite 1600
Irvine, CA 92614
949/567-6700 X 7740 Telephone
949/567-6710 Facsimile